AMENDMENT TO THE CLAIMS

Claim 1. (Currently amended) A method of promoting the healing of a skin wound comprising applying to said skin wound an effective skin wound healing amount of a composition comprising:

~~a~~ BP (bone protein mixture) depleted of histones and/or ribosomes~~,~~ and comprising

the growth factors BMP-3 and TGF-β2, and

a pharmaceutically acceptable carrier.

Claim 2. (Previously presented) The method of claim 1 wherein the composition further comprises at least one bone-derived growth factor selected from the group consisting of BMP-2, BMP-4, BMP-5, BMP-6, and BMP-7, wherein at least one said growth factor retains native post-translation modifications.

Claim 3. (Previously presented) The method of claim 1 wherein the composition further comprises at least one bone-derived growth factor selected from the group consisting of FGF-1, TGF-β1, and TGF-β3 in its native post-translation modified form.

Claim 4. (Previously presented) The method of claim 1 wherein at least one said growth factor is at least partially phosphorylated and glycosylated.

Claim 5. (Previously presented) The method of claim 1, wherein said composition is free of histone proteins H1c and H1x.

Claim 6. (Previously presented) A method of promoting skin wound healing comprising applying to said skin wound a composition comprising a mixture of growth factors comprising BMP-2, BMP-3, BMP-6, and TGF-β2 in a pharmaceutically acceptable carrier.

Claim 7. (Previously presented) The method of claim 1 wherein said composition is substantially free of ribosomal proteins LORP, Lg, s20, L3, S3a, S4 and L32.

Claim 8. (Previously presented) The method of claim 1 wherein said at least one growth factor is derived from bovine bone and is at least partially phosphorylated and glycosylated.

Claim 9. (Currently amended) A composition for the treatment of skin wounds comprising:

~~a~~ histone-depleted BP (bone protein mixture) comprising~~;~~

at least one growth factor retaining native post-translation modifications~~;~~ and

BMP-3 and TGF-β2; and

a pharmaceutically acceptable carrier, wherein said composition is active for promoting skin wound healing without inducing osteogenesis when implanted at a site in need of skin wound healing.

Claim 10. (Previously presented) The composition of claim 9, wherein said histone-depleted bone protein mixture has been further treated to remove ribosomal proteins.

Claim 11. (Currently amended) A composition for the treatment of skin wounds comprising:

~~a~~ ribosome-depleted BP (bone protein mixture) comprising~~,~~

at least one bone morphogenetic protein retaining native port-translation modifications~~;~~ and

BMP-3 and TGF-β2; and

a pharmaceutically acceptable carrier, wherein said composition is active for promoting skin wound healing without inducing osteogenesis when implanted at a site in need of skin wound healing.

Claim 12. (Previously presented) The composition of claim 11, wherein said ribosome-depleted bone protein mixture has been further treated to remove histone proteins.

Claim 13. (Currently amended) A composition for the treatment of skin wounds comprising:

~~a~~ BP (bone protein mixture) depleted of histones and/or ribosomes~~,~~ and comprising

the growth factors BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF-β1, TGF-β2, TGF-β3, and FGF-1, each retaining native post-translation modifications; and

a pharmaceutically acceptable carrier, wherein said composition is active for promoting skin wound healing without inducing osteogenesis when implanted at a site in need of skin wound healing.

Claim 14. (Original) The composition of claim 13, wherein ribosomal proteins have been substantially eliminated from the bone protein mixture.

Claim 15. (Original) The composition of claim 13, wherein histone proteins have been substantially eliminated from the bone protein mixture.

Claim 16. (Previously presented) The composition of claim 13, wherein said proteins are at least partially phosphorylated and glycosylated.

Claim 17. (Previously presented) The composition of claim 13, further comprising at least one recombinantly produced protein chosen from the group consisting of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF-β1, TGF-β2, TGF-β3 and FGF-l.

Claim 18. (Previously presented) A method of promoting the healing of a skin wound, said method comprising applying to a skin wound a composition comprising a bone-derived mixture of proteins comprising BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF-β1, TGF-β2, TGF-β3 and FGF-1 in a pharmaceutically acceptable carrier.

Claim 19. (Original) The method of claim 18, wherein the pharmaceutically acceptable carrier includes a hydrogel.

Claim 20. (Previously presented) The method of claim 18, wherein said proteins are at least partially phosphorylated and glycosylated.

Claim 21. (Original) The method of claim 18, where the pharmaceutically acceptable carrier includes a dressing selected from the group consisting of hydrocolloid dressings, hydrogels, foam dressings, and alginate dressings.

Claim 22. (Previously presented) The method of claim 18, wherein said composition further comprises one or more active ingredient selected from the group consisting of arginine, glutamine, zinc, copper, vitamin C, vitamin Bl, vitamin B2, vitamin B3, vitamin B6, vitamin B 12, and folate.

Claim 23. (Previously presented) The method of claim 18, wherein said composition further comprises one or more growth factor selected from the group consisting of epidermal growth factor, platelet derived growth factor, insulin-like growth factor, keratinocyte growth factor, vascular endothelial growth factor, transforming growth factor alpha, nerve growth factor, connective tissue growth factor and granulocyte-monocyte colony stimulating factor.

Claim 24. (Previously presented) The composition of claim 11, further including one or more inflammation inhibitor selected from the group consisting of interleukin-l inhibitor, interleukin-6 inhibitor and tumor necrosis factor-alpha inhibitor.

Claim 25. (Canceled)

Claim 26. (Previously presented) A method of improving angiogenesis in a wound area where osteogenesis is not desired comprising applying to said wound a composition comprising a bone protein mixture, wherein when said mixture is subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis, yields a reduced or non-reduced protein band pattern as identified in Figure 1, said composition including a pharmaceutically acceptable carrier.

Claim 27. (Previously presented) The composition of claim 11 comprising the growth factors BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF-β1, TGF-β2, TGF-β3, and FGF-l.

Claim 28. (Currently amended) The method of claim 1 wherein said bone protein mixture is obtained from bovine bone, and, when subjected to trypsin digestion, comprises the following tryptic peptide fragments:

XLAAAGYDVEK (SEQ ID NO:1)

SLEKVCADLIR (SEQ ID NO:2)

(V)VCGMLGFPSEAPV (SEQ ID NO:3)

STGVLLPLQNNELPG (SEQ ID NO:4)

STGVLLPLQNNELPGAEYQY (SEQ ID NO:5)

STGVLLPLQ (SEQ ID NO:6)

(S)QTLQFXE (SEQ ID NO:7)

VYAF (SEQ ID NO:8)

HAGKYSREKNT(P)A(P) (SEQ ID NO:9)

SQTLQFDEQ (SEQ ID NO:10)

SLKPSNHA (SEQ ID NO:11)

A(H)I(Q)VERYV (SEQ ID NO:12)

XALF(G)AQLGXALGPI (SEQ ID NO:13)

SQTLQFDEQT (SEQ ID NO:14)

SQTLXF (SEQ ID NO:15)

VLATVTKPVGGDK (SEQ ID NO:16)

xVFAL (SEQ ID NO:17)

AVPQLQGYLR (SEQ ID NO:18)

ALDAAYCFR (SEQ ID NO:19)

GYNANFCAGACPYL (SEQ ID NO:20)

VNSQSLSPY (SEQ ID NO:21)

KAAKPSV(P) (SEQ ID NO:22).

Claim 29. (Previously presented) The method of claim 1 wherein said skin wound comprises a diabetic ulcer.

Claim 30. (New) A composition comprising:

a mixture of growth factors comprising BMP-2, BMP-3, BMP-6, and TGF-β2 in a pharmaceutically acceptable carrier.

Claim 31. (New) A composition comprising:

a bone-derived mixture of proteins comprising BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF-β1, TGF-β2, TGF-β3 and FGF-1 in a pharmaceutically acceptable carrier.

Claim 32. (New) A composition comprising:

a bone protein mixture in a pharmaceutically acceptable carrier, wherein when said mixture is subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis it yields a reduced or non-reduced protein band pattern as identified in Figure 1.

Claim 33. (New) The method of claim 1, wherein the BP is prepared by a process comprising protein extraction from demineralized bone, filtration, and chromatography.

Claim 34. (New) The method of claim 33, wherein the filtration comprises first ultrafiltration with an ultrafiltration membrane having a nominal molecular weight cut off (MWCO) of 100 kD, to yield a retentate and a filtrate, and second ultrafiltration of the filtrate with an ultrafiltration membrane having a nominal MWCO of about 10 kD.

Claim 35. (New) The method of claim 33, wherein the chromatography comprises anion exchange chromatography, cation exchange chromatography, and HPLC in which the BP is eluted from the column with an organic solvent/water mixture gradient.

Claim 36. (New) The method of claim 1, wherein the bone protein mixture is extracted from demineralized bone.

Claim 37. (New) The method of claim 1, wherein selected proteins are excluded from the bone protein mixture.

Claim 38. (New) The method of claim 1, wherein when the bone protein mixture is subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis it yields a reduced or non-reduced protein band pattern as identified in any one of Figures 1-6.

Claim 39. (New) The method of claim 36, wherein the bone protein mixture is subjected to chromatography.

Claim 40. (New) The method of claim 39, wherein the bone protein mixture comprises at least one fraction eluted during chromatography.

Claim 41. (New) The method of claim 9, wherein the BP is prepared by a process comprising protein extraction from demineralized bone, filtration, and chromatography.

Claim 42. (New) The method of claim 41, wherein the filtration comprises first ultrafiltration with an ultrafiltration membrane having a nominal molecular weight cut off

(MWCO) of 100 kD, to yield a retentate and a filtrate, and second ultrafiltration of the filtrate with an ultrafiltration membrane having a nominal MWCO of about 10 kD.

Claim 43. (New) The method of claim 41, wherein the chromatography comprises anion exchange chromatography, cation exchange chromatography, and HPLC in which the BP is eluted from the column with an organic solvent/water mixture gradient.

Claim 44. (New) The method of claim 9, wherein the bone protein mixture is extracted from demineralized bone.

Claim 45. (New) The method of claim 9, wherein selected proteins are excluded from the bone protein mixture.

Claim 46. (New) The method of claim 9, wherein when the bone protein mixture is subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis it yields a reduced or non-reduced protein band pattern as identified in any one of Figures 1-6.

Claim 47. (New) The method of claim 44, wherein the bone protein mixture is subjected to chromatography.

Claim 48. (New) The method of claim 47, wherein the bone protein mixture comprises at least one fraction eluted during chromatography.

Claim 49. (New) The method of claim 11, wherein the BP is prepared by a process comprising protein extraction from demineralized bone, filtration, and chromatography.

Claim 50. (New) The method of claim 49, wherein the filtration comprises first ultrafiltration with an ultrafiltration membrane having a nominal molecular weight cut off (MWCO) of 100 kD, to yield a retentate and a filtrate, and second ultrafiltration of the filtrate with an ultrafiltration membrane having a nominal MWCO of about 10 kD.

Claim 51. (New) The method of claim 49, wherein the chromatography comprises anion exchange chromatography, cation exchange chromatography, and HPLC in which the BP is eluted from the column with an organic solvent/water mixture gradient.

Claim 52. (New) The method of claim 11, wherein the bone protein mixture is extracted from demineralized bone.

Claim 53. (New) The method of claim 11, wherein selected proteins are excluded from the bone protein mixture.

Claim 54. (New) The method of claim 11, wherein when the bone protein mixture is subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis it yields a reduced or non-reduced protein band pattern as identified in any one of Figures 1-6.

Claim 55. (New) The method of claim 52, wherein the bone protein mixture is subjected to chromatography.

Claim 56. (New) The method of claim 55, wherein the bone protein mixture comprises at least one fraction eluted during chromatography.

Claim 57. (New) The method of claim 13, wherein the BP is prepared by a process comprising protein extraction from demineralized bone, filtration, and chromatography.

Claim 58. (New) The method of claim 57, wherein the filtration comprises first ultrafiltration with an ultrafiltration membrane having a nominal molecular weight cut off (MWCO) of 100 kD, to yield a retentate and a filtrate, and second ultrafiltration of the filtrate with an ultrafiltration membrane having a nominal MWCO of about 10 kD.

Claim 59. (New) The method of claim 57, wherein the chromatography comprises anion exchange chromatography, cation exchange chromatography, and HPLC in which the BP is eluted from the column with an organic solvent/water mixture gradient.

Claim 60. (New) The method of claim 13, wherein the bone protein mixture is extracted from demineralized bone.

Claim 61. (New) The method of claim 13, wherein selected proteins are excluded from the bone protein mixture.

Claim 62. (New) The method of claim 13, wherein when the bone protein mixture is subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis it yields a reduced or non-reduced protein band pattern as identified in any one of Figures 1-6.

Claim 63. (New) The method of claim 60, wherein the bone protein mixture is subjected to chromatography.

Claim 64. (New) The method of claim 63, wherein the bone protein mixture comprises at least one fraction eluted during chromatography.